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Investigation in the field of quinazolines. 8*. New reaction of *N*-alkylation of 4,4-diphenyl-3,4-dihydroquinazolines

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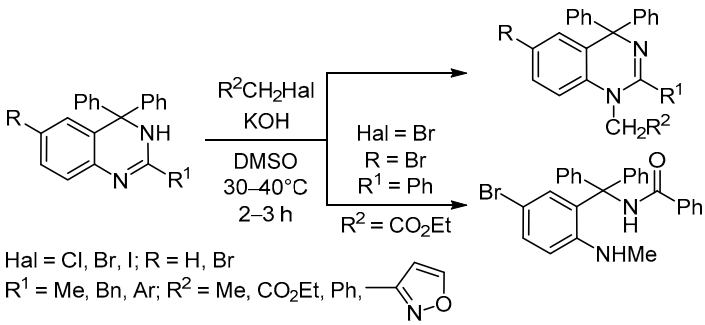


The reaction of substituted 4,4-diphenyl-3,4(1,4)-dihydroquinazolines with various alkylating agents in DMSO–KOH leads (depending on the structure of the alkylating agent) to the formation of the corresponding N^1-monoalkyl-substituted 1,4-dihydroquinazolines or, in the reaction with ethyl bromoacetate, to *N*-{[5-bromo-2-(methylamino)phenyl]diphenylmethyl}benzamide with opening of the heterocyclic ring. The molecular structures of 1-ethyl-2,4,4-triphenyl-1,4-dihydroquinazoline and 1-ethyl-2-(7-methoxy-1,3-benzodioxol-5-yl)-4,4-diphenyl-1,4-dihydroquinazoline were investigated and proven by X-ray structural analysis.

Keywords: *N*-{[5-bromo-2-(methylamino)phenyl]diphenylmethyl}benzamide, dimethyl sulfoxide, 4,4-diphenyl-3,4-dihydroquinazolines, N^1-substituted 4,4-diphenyl-1,4-dihydroquinazolines, alkylation, molecular structure.

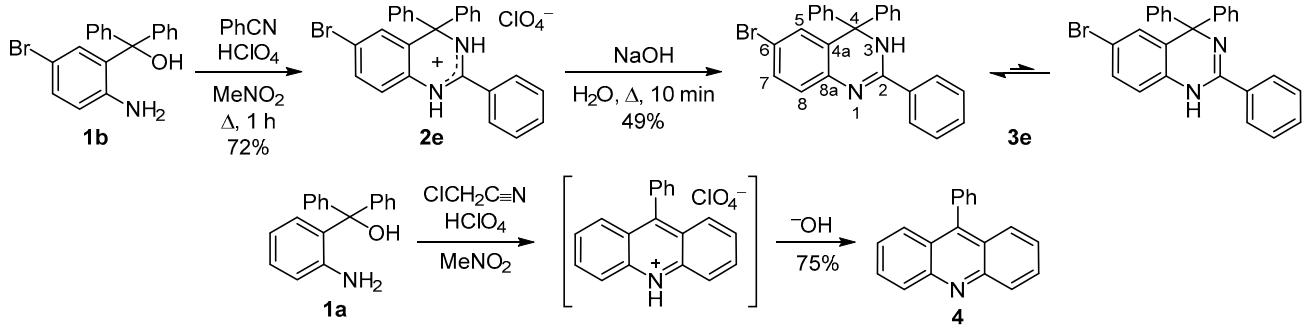
This work is a continuation of our research on 3,4-dihydroquinazoline derivatives and the study of their properties. We have previously developed a method for the preparation of 2,4-substituted 3,4-dihydroquinazolines by the reaction of (2-aminophenyl)diphenylmethanol with nitriles *via* the corresponding perchlorates.[2,3] The existence of 3,4-dihydroquinazolines in equilibrium with the tautomeric 1,4-dihydro form in solution was revealed.[4] The possibility of prototropic rearrangement into tetrahydroquinazolines was found for a number of structures containing an active methylene unit directly bonded with the heterocyclic ring.[2,4,5]

The expediency of continued research in the field of quinazolines is determined by the discovery of derivatives with pharmacological activity among them.[6–16] We have also shown that the search for antidotes to the action of the herbicide 2,4-D[17,18] used in agriculture among quinazoline derivatives shows promise. Therefore, the goal of this work was, on the one hand, to study the direction of the heterocycle alkylation process and, on the other hand, to introduce functional groups with a potential for high biological activity as a result of alkylation at a certain position of the quinazoline ring.

To expand the number of investigated structures, 6-bromo-2,4,4-triphenyl-3,4-dihydroquinazoline (**3e**) was synthesized *via* the corresponding perchlorate **2e** from

* For Communication 7, see [1].

Scheme 1

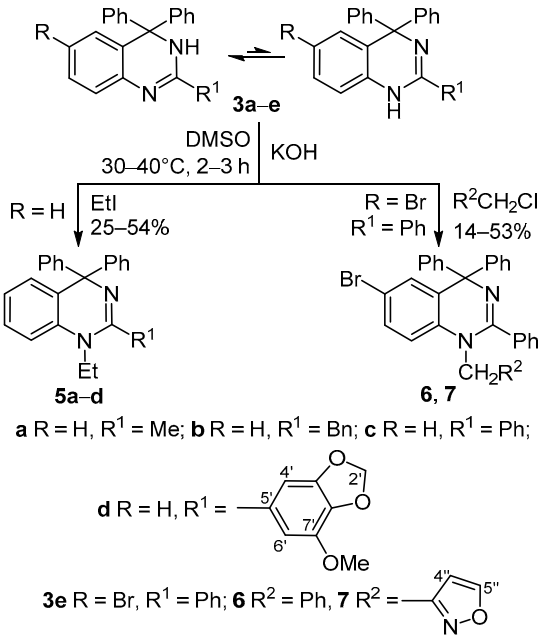


(2-amino-5-bromophenyl)diphenylmethanol (**1b**) according to a previously developed method[2,3] (Scheme 1). An attempt to obtain 2-chloromethyl-4,4-diphenyl-3,4-dihydroquinazoline by the reaction of (2-aminophenyl)diphenylmethanol (**1a**) with chloroacetonitrile under the same conditions[2,3] led to the previously described[19] phenylacridine (**4**) in 75% yield.

It was shown in our previous reports[1–5] that alkylation of 3,4-dihydroquinazolines with highly active Me_2SO_4 always proceeds as dimethylation at both nitrogen atoms of the heterocycle with the formation of the corresponding quinazolinium salts which decompose upon treatment with H_2O with opening of the heterocyclic ring to give the corresponding aminoamides. The use of the less active MeI (in Me_2CO in the presence of solid KOH) made it possible to obtain the products of monomethylation at the N-1 nitrogen atom. However, attempts to use other alkyl halides as alkylating agents were unsuccessful. Replacing the Me_2CO solvent with the more ionizing and nucleophile-activating DMSO makes it possible to obtain monoalkylation products **5a**–**d**, **6**, **7** using a variety of alkylating agents (Scheme 2).

The reaction of 6-bromo-2-phenyl-3,4-dihydroquinazoline (**3e**) with ethyl bromoacetate is an exception. Instead of the expected ethyl (6-bromo-2,4,4-triphenylquinazolin-1(4*H*)-yl)acetate, *N*-{[5-bromo-2-(methylamino)phenyl]diphenylmethyl}benzamide (**8**) was obtained according to IR spectroscopy, NMR spectroscopy, and mass spectrometry. In the ^1H and ^{13}C NMR spectra of compound **8**, no signals of the ethoxycarbonyl group are present, but there are signals of the NCH_3 group and two singlet signals of protons not bonded to carbon atoms (according to the ^1H–^{13}C HSQC spectrum). In the high-resolution mass spectrum, a peak of the radical cation $[M–CH_3OH]^+$ can be observed formed as a result of one of the two classical processes of molecular ion fragmentation, a rearrangement process with extrusion of a neutral small molecule, in this case MeOH.

Scheme 2



A possible route for the formation of compound **8** is shown in Scheme 3 as a working hypothesis and involves the hydrolysis of the ester group, decarboxylation, and opening of the heterocycle during the isolation of the product in an alkaline aqueous medium. The question of the sequence of the steps of hydrolysis of the ester group and opening of the heterocycle remains open so far.

The IR spectra of compounds **5a**–**d**, **6**, **7** contain absorption bands at 1590–1630 cm^{-1}, which are characteristic of stretching vibrations of the azomethine group, which indicates that the heterocyclic ring remains intact. In the ^1H NMR spectra, there are signals of the protons of the NCH_2 groups in the range of 3.60–3.75 ppm in the form of quartets for dihydroquinazolines **5a**–**d** and singlets at 4.75 and 4.85 ppm for dihydroquinazolines **6**, **7**, respectively.

Scheme 3

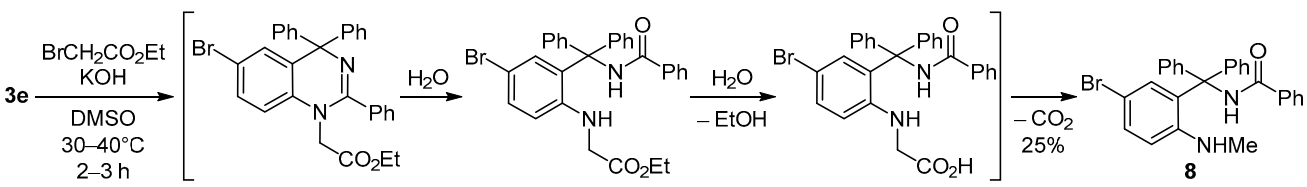


Table 1. Results of heteronuclear correlation experiments (^{1}H–^{13}C HSQC and ^{1}H–^{13}C HMBC spectra) for compound **5d**

Proton	Signals of ^{1}H nuclei, δ, ppm	Signals of ^{13}C nuclei that have cross peaks, δ, ppm	
		^{1}H–^{13}C HSQC spectrum	^{1}H–^{13}C HMBC spectrum
$CH_2C\underline{H}_3$	0.58	13.2	41.8
NCH_2	3.69	41.8	155.6; 138.0
OCH_3	3.92	56.7	143.4
2'-CH_2	5.99	101.8	136.5; 148.7
H-8	6.66	128.8	138.0; 127.3; 67.6
H-6'	6.73	109.4	155.6; 148.7; 143.4
H-4'	6.73	103.8	136.5; 130.5

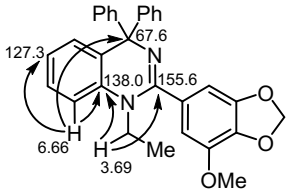


Figure 1. Structurally significant correlations in the ^{1}H–^{13}C HMBC spectrum of compound **5d**.

The presence in the IR spectrum of product **8** of characteristic vibration bands of the amide group at 1640 and 3100 cm^{-1} and broadened singlets of the NH protons of the amine and amide groups (at 1.80 and 6.18 ppm, respectively) in the ^{1}H NMR spectrum indicates the opening of the heterocycle.

In the ^{1}H–^{13}C HMBC correlation spectrum (Table 1) of compound **5d**, a characteristic cross peak can be observed at 3.69/138.0 ppm confirming the spin interaction of the methylene group protons with the C-8a carbon atom, which is possible when the ethyl group is located at the N-1 atom but not at the N-3 atom (Fig. 1).

Earlier[1] and in the present study, we have shown by NMR spectroscopy that methylation and ethylation of 2-aryl-4,4-diphenylquinazolines occurs at the N-1 nitrogen atom. To unambiguously prove the direction of the alkylation process of compounds **3a**–**d** and the spatial structure of the alkylation products **5a**–**d**, **6**, **7**, X-ray structural analysis of single crystals of 1-ethyl-2,4,4-triphenyl-1,4-dihydroquinazoline (**5c**) and 1-ethyl-2-(7-methoxy-1,3-benzodioxol-5-yl)-4,4-diphenyl-1,4-dihydroquinazoline (**5d**) was carried out (Fig. 2). As can be seen, alkylation actually occurs at position 1 of the quinazoline ring, apparently due to steric hindrances during electrophilic attack at position 3.

In both molecules, ring B is not planar – it has a twist-boat conformation. Atoms N(1) and C(4) exit the plane of the benzene ring A in different directions (atom N(1) by –0.17 and atom C(4) by 0.17 Å), the C (2) and N (3) atoms exit in the direction of atom C(4) by about 0.7 Å. For molecule **5c**, the "bottom" of the boat of ring B formed by the atoms C(2), N(3), C(4a), and C(8a) is an almost ideal plane (the average deviation of atoms from the plane is 0.0065 Å). The "walls" of the boat N(3)–C(4)–C(4a) and C(8a)–N(1)–C(2) deviate from the plane of the "bottom" of the boat by approximately the same angles 20.3 and 19.6°, respectively. The geometry of ring B of molecule **5d** is almost identical to that described above. The nitrogen atom N(1) of both molecules has a planar environment: the sum of the bond angles for this nitrogen atom is 360°. The lengths of the N(1)–C(8a) and N(1)–C(2) bonds differ markedly: the N(1)–C(2) bond is by 0.02 Å shorter than the N(1)–C(8a) bond, that is, the conjugation of the lone pair of nitrogen atoms N(1) is more directed toward the electron-withdrawing azomethine unit.

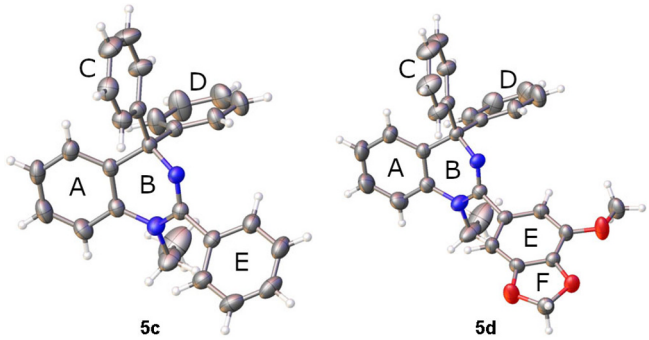


Figure 2. Molecular structures of compounds **5c**,**d** with atoms represented as thermal vibration ellipsoids of 50% probability.

The mutual arrangement of the benzene ring A and phenyl substituents C and D at the C(4) atom resembles that of the triphenylmethane molecule.[20–24] In this case, the conformation is most easily characterized by the rotation of rings A, C, and D relative to the planes N(3)–C(4)–C(5), N(3)–C(4)–C(1'C), and N(3)–C(4)–C(1'D), respectively. The angles of rotation of ring A relative to the plane N(3)–C(4)–C(5) are 41.4° in molecule **5c** and 41.1° in molecule **5d**. Ring C is rotated relative to plane N(3)–C(4)–C(1'C) by 48.9 and 49.1°, ring D is rotated relative to plane N(3)–C(4)–C(1'D) by 40.1 and 37.4° in molecules **5c** and **5d**, respectively. In the latter case, the rotation of ring D is possibly influenced by a change in the volume of the substituent at the C-7' atom. On the whole, both molecules have a conformational arrangement of rings A, C, and D called the "distorted propeller".[21–24]

The bicyclic system EF of molecule **5d** is planar, the average deviation from the plane does not exceed 0.0089 Å. The oxygen atom of the methoxy group is located in this plane, the methoxy group itself is turned in the opposite direction from the ethyl substituent toward ring D.

The positions of the aryl substituents E (compound **5c**) and EF (compound **5d**) at the C(2) atom are most easily characterized by the values of the torsion angles N(3)–C(2)–C(1'E)–C(2'E) and N(3)–C(2)–C(5'EF)–C(6EF), which are 47.9 and 70.8°, respectively. And again, in the latter case, the change in the angle is obviously associated with a change in the volume of the substituent and its contact with the phenyl substituent D.

To conclude, new conditions have been developed for the preparation of *N*^{1}-monoalkyl-substituted 1,4-dihydroquinazolines based on 3,4-dihydroquinazolines and various alkylating agents in DMSO.

Experimental

IR spectra were registered on a PerkinElmer SpectrumTwo spectrometer using the attenuated total reflectance (ATR) accessory. ^{1}H and ^{13}C NMR spectra were acquired on an Agilent 400/54 spectrometer (400 and 100 MHz, respectively) in DMSO-d_6 and $CDCl_3$, using TMS as internal standard. High-resolution mass spectra were recorded on a Bruker maXis^{TM} Impact UHR/Q-TOF mass spectrometer (electrospray ionization). Elemental analysis was performed on a Hewlett-Packard HP-185B CHN-analyzer. Melting points were determined on a Stuart SMO 30 apparatus. Monitoring of the reaction progress was done by TLC on Silufol UV-254 plates (PhH–Me_2CO, 9:1 for compounds **5a**–**d** and PhH for compounds **2e**, **3e**, **6**–**8**), visualization with iodine vapor.

The starting compounds **3a**–**e** were obtained according to published methods,[3,4] their physicochemical characteristics correspond to those described earlier.[2,5]

6-Bromo-2,4,4-triphenyl-3,4-dihydroquinazolinium perchlorate (2e) was synthesized according to a literature method[3] from (2-amino-5-bromophenyl)diphenylmethanol (**1b**) (0.283 g, 0.8 mmol), PhCN, and $HClO_4$. Yield 0.315 g (72%), light-yellow crystals, mp 245–250°C. IR spectrum, ν, cm^{-1}: 1075 (ClO_4^-), 1110 (ClO_4^-), 1650, 3220. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 6.76 (1H, d, *J* = 7.8, H-8); 7.16–7.30 (4H, m, H Ar); 7.37–7.58 (6H, m, H Ar); 7.60–7.82 (5H, m, H Ar); 7.90–7.95 (2H, m, H-2,6 2-Ph); 11.92 (1H, s, NH); 12.80 (1H, br. s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 67.1 (C-4); 119.4 (C-6); 120.2 (C Ar); 126.6 (C Ar); 127.1 (C Ar); 128.6 (4C Ar); 129.2 (C Ar); 129.3 (4C Ar); 129.5 (2C Ar); 130.1 (2C Ar); 131.2 (C-8); 131.5 (C Ar); 132.7 (C Ar); 133.2 (2C Ar); 135.0 (C Ar); 142.8 (C-8a); 157.3 (C-2). Found, *m*/*z*: 439.0828. $[M+H]^+$. $C_{26}H_{20}BrN_2$. Calculated, *m*/*z*: 439.0804.

6-Bromo-2,4,4-triphenyl-3,4(1,4)-dihydroquinazoline (3e) was obtained by deprotonation of salt **2e**. Salt **2e** (390 mg, 0.73 mmol) was mixed with an excess of 5% aqueous NaOH (10–15 ml), and the mixture was heated under reflux for 10 min. Then the mixture was cooled, the precipitate was filtered off, washed with H_2O, dried, and recrystallized from EtOH. Yield 158 mg (49%), colorless crystals, mp 220–222°C, R_f 0.17. IR spectrum, ν, cm^{-1}: 1620 (C=N), 3352 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 3.35 (1H, br. s, NH); 6.70 (1H, d, *J* = 7.2, H-8); 7.20–7.33 (5H, m, H Ph); 7.35–7.42 (7H, m, H Ph, H-5,7); 7.62–7.64 (3H, m, H-3,4,5 2-Ph); 7.93–7.95 (2H, m, H-2,6 2-Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 67.3 (C-4); 115.2 (C-6); 117.5 (C Ar); 126.7 (2C Ar); 127.1 (C Ar); 127.4 (C Ar); 127.9 (4C Ar); 128.2 (2C Ar); 128.9 (4C Ar); 129.3 (2C Ar); 129.6 (2C Ar); 130.3 (C Ar); 131.2 (C Ar); 135.0 (C-4a); 144.3 (C-8a); 157.4 (C-2). Found, *m*/*z*: 439.0817 $[M+H]^+$. $C_{26}H_{20}BrN_2$. Calculated, *m*/*z*: 439.0804.

Synthesis of compounds 5a–d, 6–8 (General method). The corresponding 3,4(1,4)-dihydroquinazoline **3a**–**e** (0.32 mmol) and alkylating agent (0.64 mmol) were successively added with stirring to a mixture of KOH powder (72 mg, 1.3 mmol) and DMSO (5 ml). The reaction was carried out at 30–40°C for 2–3 h (TLC control). Then, H_2O (20–25 ml) was added to the reaction mixture. The formed precipitate was extracted with CH_2Cl_2 (3×10 ml), the organic extracts were combined and dried over anhydrous Na_2SO_4. After filtration and distillation of the solvent, the solid residues were recrystallized from EtOH.

1-Ethyl-2-methyl-4,4-diphenyl-1,4-dihydroquinazoline (5a). Yield 53 mg (51%), colorless crystals, mp 136–138°C, R_f 0.11. IR spectrum, ν, cm^{-1}: 1630 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.09 (3H, t, *J* = 6.6, CH_3); 2.31 (3H, s, 2-CH_3); 3.75 (2H, q, *J* = 6.6, CH_2); 6.63 (1H, dd, *J* = 7.2, *J* = 1.2, H-8); 6.93–6.97 (2H, m, H-5,7); 7.13–7.39 (11H, m, H Ph, H-6). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.5 ($CH_2\underline{C}H_3$); 21.6 (2-CH_3); 39.9 (CH_2); 66.2 (C-4); 111.4 (C Ar); 122.2 (C Ar); 126.3 (2C Ar); 127.3 (C Ar); 127.4 (4C Ar);127.8 (C Ar); 128.8 (4C Ar); 129.1 (2C Ar); 137.3 (C Ar); 148.1 (C Ar); 152.6 (C-2). Found, %: C 84.52; H 6.79; N 8.53. $C_{23}H_{22}N_2$. Calculated, %:C 84.63; H 6.79; N 8.58.

2-Benzyl-1-ethyl-4,4-diphenyl-1,4-dihydroquinazoline (5b). Yield 58 mg (45%) colorless crystals, mp 172–174°C, R_f 0.41. IR spectrum, ν, cm^{-1}: 1610 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.86 (3H, t, *J* = 7.3, CH_3); 3.60 (2H, q, *J* = 7.3, NCH_2); 4.00 (2H, s, CH_2); 6.63 (1H, dd, *J* = 8.2, *J* = 2.0, H-8); 6.91–6.98 (1H, m, H Ar); 6.98–7.00 (2H, m, H Ar); 7.15–7.20 (5H, m, H 2-$CH_2\underline{Ph}$); 7.26–7.28 (10H, m, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.5 (CH_3); 39.5 (CH_2); 41.3 (NCH_2); 67.0 (C-4); 111.6 (C Ar); 122.6 (C Ar); 126.4 (2C Ar); 127.4 (2C Ar); 127.5 (4C Ar); 127.7 (C Ar); 127.9 (2C Ar); 128.5 (2C Ar); 129.0 (4C Ar); 129.1 (2C Ar); 137.2 (C Ar); 137.4 (C Ar); 147.8 (C Ar); 154.0 (C-2). Found, %: C 86.50; H 6.41; N 6.71. $C_{29}H_{26}N_2$. Calculated, %: C 86.53; H 6.51; N 6.96.

1-Ethyl-2,4,4-triphenyl-1,4-dihydroquinazoline (5c). Yield 67 mg (54%), colorless crystals, mp 208–210°C, R_f 0.79. IR spectrum, ν, cm^{-1}: 1600 (C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 0.38 (3H, t, *J* = 6.8, CH_3); 3.67 (2H, q, *J* = 6.8, NCH_2); 6.55 (1H, dd, *J* = 6.5, *J* = 1.2, H-8); 7.04–7.29 (12H, m, H Ph, H-5,7); 7.38 (1H, ddd, *J* = 6.6, *J* = 6.5, *J* = 1.2, H-6); 7.46–7.58 (5H, m, H Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.9 (CH_3); 41.7 (CH_2); 67.3 (C-4); 107.0 (C Ar); 114.2 (C Ar); 123.1 (C Ar); 126.8 (2C Ar); 127.8 (4C Ar); 128.0 (2C Ar); 128.8 (4C Ar); 129.6 (2C Ar); 129.8 (C Ar); 130.3 (C Ar); 135.0 (C Ar); 137.1 (C Ar); 138.4 (C Ar); 148.2 (C Ar); 152.2 (C Ar); 156.1 (C-2). Found, *m*/*z*: 389.2028 $[M+H]^+$. $C_{28}H_{25}N_2$. Calculated, *m*/*z*: 389.2012.

1-Ethyl-2-(7-methoxy-1,3-benzodioxol-5-yl)-4,4-diphenyl-1,4-dihydroquinazoline (5d). Yield 37 mg (25%), colorless crystals, mp 185–187°C, R_f 0.72. IR spectrum, ν, cm^{-1}: 1046–1138 (OCH_2O); 1630 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.58 (3H, t, *J* = 6.0, CH_3); 3.69 (2H, q, *J* = 6.0, NCH_2); 3.92 (3H, s, OCH_3); 5.99 (2H, s, OCH_2O); 6.66 (1H, d, *J* = 7.5, H-8); 6.73 (2H, s, H-4',6'); 7.05–7.35 (13H, m, H Ph, H-5,6,7). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.7 (CH_3); 41.8 (NCH_2); 56.7 (OCH_3); 67.6 (C-4); 101.8 (C-2'); 103.8 (C-4'); 109.4 (C-6'); 113.1 (C-5); 122.9 (C-7); 126.4 (2C Ar); 127.3 (C-6); 127.4 (4C Ar); 128.8 (C-8); 128.9 (4C Ar); 130.3

(2C Ar); 130.5 (C-5'); 136.5 (C-7a'); 138.0 (C-8a); 143.4 (C-7'); 148.0 (C-4a); 148.7 (C-3a'); 155.6 (C-2). Found, *m*/*z*: 463.2020 $[M+H]^+$. $C_{30}H_{27}N_2O_3$. Calculated, *m*/*z*: 463.2016.

1-Benzyl-6-bromo-2,4,4-triphenyl-1,4-dihydroquinazoline (6). Yield 89 mg (53%), colorless crystals, mp 203–205°C, R_f 0.31. IR spectrum, ν, cm^{-1}: 1610 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.75 (2H, s, CH_2); 6.47–6.49 (2H, m, H-2,6 1-CH_2Ph); 6.76 (1H, s, H-5); 6.82 (1H, dd, *J* = 6.5, *J* = 1.2, H-8); 6.92–6.94 (2H, m, H-3,5 1-CH_2Ph); 6.98–7.11 (1H, m, H-4 1-CH_2Ph); 7.16–7.34 (11H, m, H Ph, H-7); 7.37–7.44 (3H, m, H-3,4,5 2-Ph); 7.45–7.50 (2H, m, H-2,6 2-Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 51.2 (NCH_2); 67.4 (C-4); 114.7 (C-8); 115.5 (C-6); 126.6 (2C Ar); 126.9 (2C Ar); 127.1 (C Ar); 127.9 (4C Ar); 128.3 (2C Ar); 128.5 (2C Ar); 128.8 (2C Ar); 128.9 (4C Ar); 129.6 (C Ar); 130.3 (2C Ar); 131.1 (C Ar); 131.5 (2C Ar); 136.4 (C Ar); 137.0 (C Ar); 147.3 (C Ar); 155.5 (C-2). Found, *m*/*z*: 529.1271 $[M+H]^+$. $C_{33}H_{26}BrN_2$. Calculated, *m*/*z*: 529.1274.

3-[(6-Bromo-2,4,4-triphenylquinazolin-1(4*H*)-yl)methyl]-isoxazole (7). Yield 23 mg (14%), colorless crystals, mp 117–120°C, R_f 0.23. IR spectrum, ν, cm^{-1}: 1590, 1630 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.85 (2H, s, NCH_2); 6.85 (1H, d, *J* = 6.0, H-8); 7.10–7.22 (2H, m, H-5,7); 7.24–7.36 (10H, m, H Ph); 7.39–7.48 (5H, m, 2-Ph); 7.85–7.88 (2H, m, H-4",5"). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 43.0 (NCH_2); 66.1 (C-4); 102.5 (C Ar); 114.6 (C-6); 126.9 (2C Ar); 127.0 (C Ar); 127.8 (2C Ar); 127.9 (2C Ar); 128.3 (4C Ar); 128.4 (C Ar); 128.7 (C Ar); 128.8 (4C Ar); 129.0 (C Ar); 130.2 (C Ar); 131.1 (C Ar); 131.5 (C Ar); 134.5 (C Ar); 145.0 (C Ar); 147.2 (C Ar); 158.5 (C-2); 167.2 (C=N). Found, *m*/*z:* 520.1012 $[M+H]^+$. $C_{30}H_{23}BrN_3O$. Calculated, *m*/*z*: 520.1019.

***N*-{[5-Bromo-2-(methylamino)phenyl]diphenylmethyl}-benzamide (8)**. Yield 37 mg (25%), colorless crystals, mp 116–118°C, R_f 0.20. IR spectrum, ν, cm^{-1}: 1640, 3100 (NHCO); 3320 ($NHCH_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.80 (1H, br. s, N<u>H</u>CH_3); 2.59 (3H, s, NHC<u>H</u>$_3$); 6.18 (1H, br. s, NHCO); 6.85 (1H, d, *J* = 7.3, H-3); 7.26–7.39 (12H, m, H Ph, H-4,6); 7.40–7.45 (3H, m, H-3,4,5 COPh); 7.83–7.86 (2H, m, H-2,6 COPh). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 40.9 ($NHCH_3$); 67.2 (CONH); 117.3 (C Ar); 122.0 (C Ar); 126.8 (4C Ar); 126.9 (C Ar); 127.7 (C Ar); 128.2 (4C Ar); 128.4 (2C Ar); 128.8 (2C Ar); 129.7 (2C Ar); 131.0 (2C Ar); 131.2 (C Ar); 133.0 (C Ar); 141.1 (C Ar); 145.5 (C Ar); 171.0 (C=O). Found, *m*/*z*: 439.0805 $[M+H–CH_3OH]^+$. $C_{27}H_{20}BrN_2$. Calculated, *m*/*z*: 439.0804.

X-ray structural analysis of compounds 5c,d. Single crystals of compounds **5c**,**d** were grown by crystallization from EtOH. Structure analysis was carried out on an Agilent SuperNova diffractometer at 100 K and using a microfocus X-ray source with a copper anode and an Atlas S2 CCD coordinate detector. The collection of reflections, determination and refinement of the unit cell parameters were carried out using the specialized software package CrysAlisPro 1.171.39.46 (RigakuOxfordDiffraction, 2018) .[25] The structures were decoded and refined using the ShelXT software (Sheldrick, 2015),[26] molecular graphics and preparation of the material for publication were performed with the software package Olex2 ver 1.2.10.[27]

Crystals of compound **5c** ($C_{28}H_{24}N_2$, *M* 388.49) are monoclinic, space group $P2_1$; *a* 7.8330(2), *b* 10.6310(3), *c* 12,8832(4) Å; β 93.420(3)°; *V* 1070.91(5) $Å^3$; *Z* 2; *T* 293 (2) K; μ(CuKα) 0.538 mm^{-1}; d_{calc} 1.205 g/cm^3. A total of 22347 reflections were collected (6.874° ≤ 2Θ ≤ 152.586°), of which 4478 were unique (R_{int} 0.0461, $R_σ$ 0.0274), which were used in all calculations. The final probability factors were R_1 0.0347 ($I > 2σ(I)$), wR_2 0.0945.

Crystals of compound **5d** ($C_{30}H_{26}N_2O_3$, *M* 462.53) are monoclinic, space group $P2_1/c$; *a* 8,81360(10), *b* 16.8898(2), *c* 16.3417(2) Å; β 92.7960(10)°; *V* 2429.73(5) $Å^3$; *Z* 4; *T* 293(2) K; μ(CuKα) 0.654 mm^{-1}; d_{calc} 1.264 g/cm^3. A total of 25125 reflections were collected (7.532° ≤ 2Θ ≤ 152.354°), of which 5045 were unique (R_{int} 0.0334, $R_σ$ 0.0189), which were used in all calculations. The final probability factors were R_1 0.0385 ($I > 2σ(I)$), wR_2 0.1024.

The full set of X-ray structural data for compounds **5c**,**d** were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 1922709 and CCDC 1922710, respectively).

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